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STATEMENT BY APPLICANT	Application Number	09/839577
(Use as many sheets as necessary)	Filing Date	April 20, 2001
/ /	First Named Inventor	Hahn, Klaus
15 CACOL 6 . 130	Group Art Unit	1653 1626
	Examiner Name	Kam. Chil Min Pobet Shid
Sheet 1 of 5	Attorney Docket No: 1	361.007US1

			US P.	ATENT DOCUMENT	S		
	Examiner Division	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	Filing Date If Appropriate
	R	US-5,268,486	12/07/1993	Waggoner, Alan S., et al.	548	427	05/15/1992
الا	g 7903	US-5,880,270	03/09/1999	Berninger, R. W., et al.	530	391.1	12/23/1997

(DEV)		<b>FOREIGN PATENT</b>	DOCUMENTS			
Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	T <sup>2</sup>

	OTHE	R DOCUMENTS NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T
100		ABDUL-MANAN, N., et al., "Structure of Cdc42 in complex with the GTPase-	
		binding domain of the 'Wiskott-Aldrich syndrome' protein.", Nature. 399(6734). (1999),379-83	
1		ADAMS, S. R., et al., "Fluorescence ratio imaging of cyclic AMP in single cells", Nature. 349(6311), (1991),694-7	
		BARK, S. J., et al., "A Hightly Efficient Method for Site-Specific Modification of	
		Unprotected Peptides after Chemical Synthesis", Journal of the American	
		Chemical Society, 122, (Apr. 19, 2000),3567-3573	
		BENARD, V., et al., "Characterization of rac and cdc42 activation in	
		chemoattractant-stimulated human neutrophils using a novel assay for active	
		GTPases", <u>Journal of Biological Chemistry</u> . 274(19), (1999),13198-204	<u> </u>
		BRINKLEY, M., "A brief survey of methods for preparing protein conjugates with	İ
ŀ		dyes, haptens, and cross-linking reagents", Bioconjugate Chemistry. 3(1).	
		(1992),2-13	
		CANNE, L. E., "Extending the Applicability of Native Chemical Ligation", <u>Journal</u> of the American Chemical Society, <u>118</u> , (1996),5891-5896	
1 1		CANNE, L. E., "Total Chemical Synthesis of a Unique Transcription Factor-	
		Related Protein: cMyc-Max", <u>J. Am. Chem. Soc., 117, (1995),2998-3007</u>	
		CERVIGNI, S. E., et al., "Synthesis of Glycopeptides and Lipopeptides by	
		Chemoselective Ligation", Angew. Chem. Int. Ed. Engl., 35, (1996),1230-1232	1
		CHAMBERLAIN, C., et al., "Watching Proteins in the Wild: Fluorescence	
		Methods to Study Protein Dynamics in Living Cells", Traffic, 1, (2000),755-762	<u> </u>
1		CHUNG, C. Y., "Role of Rac in controlling the actin cytoskeleton and chemotaxis	
		in motile cells", Proceedings of the National Academy of Sciences of the United	
		States of America. 97(10), (2000),5225-30	
110		CORNISH, V. W., et al., "Site-Specific Protein Modification Using a Ketone",	
18/		Journal of the American Chemical Society, 118, (1996),8150-8151	
// > 1		COTTON, G. J., et al., "Insertion of a Synthetic Peptide into a Recombinant	]
<del>- /  </del>		Protein Framework: A Protein Biosensor", Journal of the American Chemical	<u> </u>

EXAMINER DATE CONSIDERED 50/0

PTO/SB/084(10-01)
Approved for use through 19/31/2022, OMB 561-0031
US Patent & Trademark Office: U.S. DEPARTMENT OF COMMERCE

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT	Application Number	09/839577
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			R DOCUMENTS NON PATENT LITERATURE DOCUMENTS	
OIP	Examiner Initials	Cite No 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
	[ 2V/)		Society, 121, (1999),1100-1101	
OCT 0 9 20	03 (1)		DAWSON, P. E., "Synthesis of Proteins by Native Chemical Ligation", <u>Science</u> , <u>266</u> , (1994),pp. 776-779	
OCT 0 9 20	n rice		DAY, R. N., "Visualization of Pit-1 transcription factor interactions in the living cell nucleus by fluorescence resonance energy transfer microscopy.", <u>Molecular Endocrinology</u> , 12(9), (1998),1410-9	
·			ELY, C. M., et al., "A 42-kD tyrosine kinase substrate linked to chromaffin cell secretion exhibits an associated MAP kinase activity and is highly related to a 42-kD mitogen-stimulated protein in fibrobla", <u>Journal of Cell Biology.</u> 110(3), (1990),731-42	
			GAERTNER, H. F., et al., "Site-Specific Attachment of Functionalized Poly(ethylene glycol) to the Amino Terminus of Proteins", <u>Bioconjugate Chem. 7</u> , (1996),38-44	
			GIULIANO, K. A., et al., "Fluorescent protein biosensors: measurement of molecular dynamics in living cells.", <u>Annual Review of Biophysics &amp; Biomolecular Structure</u> . 24:, (1995),405-34	
			GONZALEZ, F. A., et al., "Heterogeneous expression of four MAP kinase isoforms in human tissues", FEBS Letters. 304(2-3), (1992),170-8	
			GRIFFIN, B. A., et al., "Specific covalent labeling of recombinant protein molecules inside live cells", Science. 281(5374), (1998),269-72	
			HAHN, K. M., et al., "A calcium-sensitive fluorescent analog of calmodulin based on a novel calmodulin-binding fluorophore", <u>Journal of Biological Chemistry</u> . 265(33), (1990),20335-45	
			HAHN, K., et al., "Patterns of elevated free calcium and calmodulin activation in living cells", Nature. 359(6397), (1992),736-8	
			HALL, A., "Rho GTPases and the actin cytoskeleton", Science. 279(5350), (1998),509-14	
			HAWKINS, P. T., et al., "PDGF stimulates an increase in GTP-Rac via activation of phosphoinositide 3-kinase", Current Biology. 5(4), (1995),393-403	
			ITOH, REINA E., et al., "Activation of Rac and Cdc42 Video Imaged by Fluorescent Resonance Energy Transfer-Based Single-Molecule Probes in the Membrane of Living Cells", Molecular and Cellular Biology, 22, (2002),6582-6591	
			JONESON, T., et al., "Suppression of Ras-induced apoptosis by the Rac GTPase", Molecular & Cellular Biology. 19(9), (1999),5892-901	
			KAISER, E., et al., "Color test for detection of free terminal amino groups in the solid-phase synthesis of peptides", Analytical Biochemistry, 34(2), (1970),595-8	
	13		KATZ, B. Z., et al., "Green fluorescent protein labeling of cytoskeletal structures-novel targeting approach based on leucine zippers", <u>Biotechniques</u> . 25(2), (1998),298-302	
_[	$\mathcal{I}$	1/	KENT, S. B., "Chemical Synthesis of Peptides and Proteins", Ann. Rev.	

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DATE CONSIDERED

PTO/SB/06A(10-01)
Approved for use through 10/31/2002, CMB 651-0031
US Plates & Trislament Office: U.S. DEPARTMENT OF COMMERCE

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	OTHE	R DOCUMENTS NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Τ²
///	ļ	Biochem., 57, (1988),957-989	<u> </u>
W'		KIM, A. S., et al., "Autoinhibition and activation mechanisms of the Wiskott-	1
		Aldrich syndrome protein", Nature. 404(6774), (2000),151-8	L
		KING, T. P., et al., "Preparation of protein conjugates via intermolecular	·
		hydrazone linkage", <u>Biochemistry</u> . 25(19), (1986),5774-9	L
		KJOLLER, L., et al., "Signaling to Rho GTPases", Experimental Cell Research.	i
J		<u>253(1),</u> (1999),166-79	<u> </u>
1 1		KNAUS, U. G., et al., "Purification and characterization of Rac 2. A cytosolic	ł
		GTP-binding protein that regulates human neutrophil NADPH oxidase", <u>Journal</u>	i
		of Biological Chemistry. 267(33), (1992),23575-82	<u> </u>
		KRAYNOV, V. S., et al., "Localized Rac activation dynamics visualized in living cells", Science. 290(5490), (2000),333-7	
		LELIEVRE, D., et al., "Simple and Efficient Solid-Phase Synthesis of	
		Unprotected Peptide Aldehyde for Peptide Segment Ligation", <u>Tetrahedron</u>	1
		Letters, 39, (1998),9675-9678	İ
		LEONARD, D. A., et al., "Use of a fluorescence spectroscopic readout to	
		characterize the interactions of Cdc42Hs with its target/effector, mPAK-3",	1
		Biochemistry. 36(5), (1997),1173-80	i
		MANSER, E., et al., "A brain serine/threonine protein kinase activated by Cdc42	
		and Rac1", Nature. 367(6458), (1994),40-46	1.
1 1		MARCAURELLE, L. A., et al., "Direct incorporation of unprotected ketone groups	1 "
	•	into peptides during solid-phase synthesis: Application to the one-step	
	•	modification of peptides with two different biophysical probes for FRET",	}
		<u>Tetrahedron Letters. 39(40), (1998),7279-7282</u>	
		MENARD, L., et al., "Rac1, a low-molecular-mass GTP-binding-protein with high	j
		intrinsic GTPase activity and distinct biochemical properties", European Journal	1
		of Biochemistry, 206(2), (1992),537-46	ļ
		MICHIELS, F., et al., "A role for Rac in Tiam1-induced membrane ruffling and	
<b>-</b>		invasion", Nature. 375(6529), (1995),338-40	ļ
		MIYASAKA, T., et al., "Nerve growth factor stimulates a protein kinase in PC-12	
		cells that phosphorylates microtubule-associated protein-2", <u>Journal of Biological</u>	1
<del></del>		Chemistry, 265(8), (1990),4730-5	<u> </u>
		MIYAWAKI, A., et al., "Fluorescent indicators for Ca2+ based on green	
		fluorescent proteins and calmodulin", Nature. 388(6645), (1997),882-7	ļ
		MUIR, T. W., "Expressed Protein Ligation: A General Method for Protein Engineering", PNAS USA, 95, (June 1998),6705-6710	
		MUJUMDAR, R. B., et al., "Cyanine dye labeling reagents containing	
		isothiocyanate groups", Cytometry, 10(1), (1989),11-9	
		NEL, A. E., et al., "Stimulation of MAP-2 kinase activity in T lymphocytes by anti-	1
		CD3 or anti-Ti monoclonal antibody is partially dependent on protein kinase C".	
		Journal of Immunology. 144(7), (1990),2683-9	

**EXAMINER** DATE CONSIDERED Substitute Disclosure Statement Form (PTC-1449)

- EXAMINER: Initial If reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication applicant, applicant and unique citation designation number (optional) applicant is to place a check mark here if English tanguage Translation is attached

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OIPE	First Named Inventor	Hahn, Klaus
	Group Art Unit	1553- 1626
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	OTHE	R DOCUMENTS NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
		NG, T., et al., "Imaging protein kinase Calpha activation in cells", Science. 283(5410), (1999),2085-9	
		NOBES, C. D., et al., "Rho GTPases control polarity, protrusion, and adhesion	
		during cell movement", Journal of Cell Biology, 144(6), (1999),1235-44	
		NOMANBHOY, T. K., et al., "Investigation of the GTP-binding/GTPase cycle of	
		Cdc42Hs using extrinsic reporter group fluorescence", <u>Biochemistry</u> . 35(14), (1996),4602-8	
		RABINOWITCH, EUGENE, et al., "Polymerization of dyestuffs in solution.	
		Thionine and methylene blue.", <u>Journal of the American Chemical Society, 63,</u> (1941),69-78	
		RAY, L. B., et al., "Rapid stimulation by insulin of a serine/threonine kinase in	
		3T3-L1 adipocytes that phosphorylates microtubule-associated protein 2 in vitro",	'
		Proceedings of the National Academy of Sciences of the United States of	
		America. 84(6), (1987),1502-6	
		RENARD, MARTIAL, et al., "Knowledge-Based Design of Reagentless	
		Fluorescent Biosensors from Recombinant Antibodies", <u>Journal of Molecular</u>	
<del>   </del>	<del></del>	Biology, 318, (2002),429-442	
		RICHIERI, G. V., et al., "The measurement of free fatty acid concentration with	
1 1 1		the fluorescent probe ADIFAB: a practical guide for the use of the ADIFAB probe", Molecular & Cellular Biochemistry, 192(1-2), (1999),87-94	
		RIDLEY, A. J., et al., "The small GTP-binding protein rac regulates growth factor-	
		induced membrane ruffling", Cell. 70(3), (1992),401-10	
		ROSE, K., "Facile Synthesis of Homogeneous Artificial Proteins", Journal of the	<del> </del>
		American Chemical Society, 116, (1994),30-33	
		ROSE, K., et al., "Natural peptides as building blocks for the synthesis of large	
		protein-like molecules with hydrazone and oxime linkages", Bioconjugate	
		Chemistry, 7(5), (1996),552-6	
	<del></del>	SCHNOLZER, M., et al., "In situ neutralization in Boc-chemistry solid phase	
		peptide synthesis. Rapid, high yield assembly of difficult sequences",	
	-	International Journal of Peptide & Protein Research. 40(3-4), (1992), 180-93	
		SEVERIN, K., et al., "A synthetic peptide ligase", Nature. 389(6652), (1997),706-9	
		SUBAUSTE, M. C., et al., "Rho family proteins modulate rapid apoptosis induced	
		by cytotoxic T lymphocytes and Fas", <u>Journal of Biological Chemistry</u> . 275(13), (2000),9725-33	
		TERPETSCHNIG, E., et al., "Synthesis of squaraine-N-hydroxysuccinimide	
.		esters and their biological application as long-wavelength fluorescent labels".	
		Analytical Biochemistry, 217(2), (1994), 197-204	
	-	THERIOT, J. A., et al., "Actin microfilament dynamics in locomoting cells", Nature. 352(6331), (1991),126-31	
		THOMPSON, G. et al., "Delineation of the Cdc42/Rac-Binding Domain of p21-	
		The state of the s	

**EXAMINER DATE CONSIDERED** Substitute Disclosure Statement Form (PTO-1449)

EXAMINER: Initial if reference considered, whether or not efficient is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered, include copy of this form with next compositional. I Applicant a unique citation designation number (optional) a Applicant is to place a check mark here if English language Translation is stached

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	OTHER	R DOCUMENTS NON PATENT LITERATURE DOCUMENTS	
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$\sim 2$		Activated Kinase", Biochemistry, 37, (1998), 7885-7891	
7)		TSIEN, ROGER Y., "The Green Fluorescent Protein", Annu. Rev. Biochem., 67, (1998),509-544	
1		WAHL, F., et al., "Analogues of oxytocin with an oxime bridge using	
		chemoselectively addressable building blocks", <u>Tetrahedron Letters. 37(38)</u> , (1996),6861-6864	
		WANG, Y. L., "Exchange of actin subunits at the leading edge of living	1
		fibroblasts: possible role of treadmilling", <u>Journal of Cell Biology</u> . 101(2), (1985),597-602	
		WEINER, O. D., et al., "Spatial control of actin polymerization during neutrophil chemotaxis", Nature Cell Biology. 1(2), (1999),75-81	
		WEST, W., et al., "The dimeric state of cyanine dyes", The Journal of Physical Chemistry, 69(6), (1965),1894-1903	
		WHISH, W. J., et al., "Studies on the Aminoxyalanine Methyl Ester and Its alpha- N-acetyl Derivative", Canadian Journal of Biochemistry, 48, (1970),520-522	
		WILKEN, J., et al., "Chemical protein synthesis", Current Opinion in Biotechnology. 9(4), (1998),412-26	
		YANG, T. T., et al., "Dual color microscopic imagery of cells expressing the green fluorescent protein and a red-shifted variant", Gene. 173(1 Spec No), (1996),19-23	
M		ZHOU, K., et al., "Guanine nucleotide exchange factors regulate specificity of downstream signaling from Rac and Cdc42", <u>Journal of Biological Chemistry</u> . 273(27), (1998),16782-6	

EXAMINER DATE CONSIDERED

Substitute Disclosure Statement Form (PTO-1449)